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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/028,415	12/20/2001	Annette Lasham	11000.1004c3	4245

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EXAMINER	
VIVLEMORE, TRACY ANN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 03/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/028,415	LASHAM ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2005 and 22 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6,9,14,23-25 and 28-38* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,9,14,24,25 and 28-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection not reiterated in this Action is withdrawn.

Status of the application

Claims 1-3, 6, 9, 14, 23-25 and 28-38 are pending. Claims 6, 9, 14, 24, 25 and 28-38 are currently under examination.

Election/Restrictions

Applicant's election with traverse of SEQ ID NO: 20 in the reply filed on December 12, 2005 is acknowledged. The traversal is on the ground(s) that all sequences in claims 33 and 34 are targeted to the same molecule and thus share a common utility. Applicant further states that searching all sequences in claims 33 and 34 would not constitute an undue burden. This is not found persuasive because while applicant is correct that the antisense sequences have the common utility of being complementary to the same gene sequence, they do not share a common structure and thus there is no unity of invention. Search of all sequences of claims 33 and 34 would constitute an undue burden. A search of one antisense sequence is not coextensive with other antisense sequences targeted to a different portion of the target gene.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

Claims 33-38 are objected to because of the following informalities: each of these claims contains non-elected subject matter, specifically the non-elected nucleotide sequences. Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 6, 9, 14 and 24, 25 remain rejected and new claims 28-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for increasing apoptotic cell death *in vitro* and *ex vivo* in cell culture, does not reasonably provide enablement for increasing apoptotic cell death by reducing the amount of a transcriptional regulator of apoptosis available to bind to a target polynucleotide *in vivo* in any organism. Moreover, the specification does not reasonably provide enablement for a method for treating a disease or infection in an organism.

Claims 6, 9, 14, 24, 25 and 28-38 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for increase of apoptosis *in vitro* in cells having functional p53, does not reasonably provide enablement for increase of apoptosis in all cells *in vitro*.

The method as claimed encompasses increase of apoptosis in any cell type. However, both the examples in the specification and applicant's statements on the record (see remarks submitted on 2/2/05 and the declaration of inventor Lasham submitted 8/22/05) demonstrate that the claimed method would not work in all cells. Cells must have functional p53 in order to increase apoptosis and thus not all cells are

useful in the claimed method. Thus, the claimed methods are not enabling throughout their full scope.

Response to arguments: Claim Rejections - 35 USC § 112

Applicant's attention is directed to the rejection statement, which has been modified to indicate no *in vivo* methods are enabled. This rejection is maintained for the reasons of record set forth in the office actions mailed 9/30/04 and 4/18/05, that in vivo delivery of nucleic acids for any therapeutic purpose in unpredictable. Delivery issues include not only administration, but uptake of the nucleic acid into the proper target cells and persistence of the nucleic acid in the intracellular environment long enough to have a measurable effect. The specification provides an example describing administration of antisense oligonucleotides or decoy oligonucleotides to fibrosarcoma cells in culture and transplantation of these cells as a xenograft in mice. This example does not describe *in vivo* delivery of any oligonucleotide for a therapeutic purpose.

Applicant argues that references previously submitted were not cited as evidence of activity of oligonucleotides directed againstYB-1 but intended to show that mouse model used in the specification would be predictive of *in vivo* activity in humans. Applicant is correct that therapeutics are frequently tested in mice before clinical trials in humans, but this argument is not persuasive because the basis of the rejection is not whether mouse models are predictive of results in humans, but whether *in vivo* delivery of therapeutic nucleic acids is predictable. The prior art teaches that *in vivo* delivery of nucleic acids is unpredictable and the specification does not provide any working examples to refute the teachings of the prior art.

Response to arguments: Claim Rejections - 35 USC § 102

Claims 6 and 9 remain rejected and new claim 33 is rejected under 35 U.S.C. 102(b) as being anticipated by Ohga et al.

Newly added claim 33 is rejected because the antisense plasmid used by Ohga et al. is identical to the cDNA of YB-1. Since SEQ ID NO: 20 is complementary to nucleotides within the coding region of YB-1, this sequence would exist within any cDNA of YB-1.

Applicant has provided a declaration intended to demonstrate that the cells used by Ohga et al. have a comprised p53 pathway. Applicant reasons that because YB-1 reduction causes cell death, only cells having a compromised p53 pathway would survive the antibiotic selection procedure. Although applicant has demonstrated a relationship between reduction of YB-1 and p53, this argument is not persuasive because it is likely some cells would survive even if the p53 apoptosis pathway were stimulated. The reference cited in the declaration, Lasham et al., teaches that following reduction of YB-1, 50% of cells undergo apoptosis and that the amount of apoptosis does not increase further. Thus, it is possible that the cell line produced by Ohga et al. has both a reduced level of YB-1 and a functional p53 pathway.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 9, 33, 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohga et al. in view of Branch (TIBS 1998, of record).

The claims are directed to a method of increasing apoptosis in a population of cells that may be tumor cells using antisense oligonucleotides directed to YB-1. The antisense oligonucleotide may be SEQ ID NO: 20 and this sequence may be administered in combination with other sequences.

Ohga et al. teach the inhibition of YB-1 in tumor cells using an antisense oligonucleotide. This sequence is identical to the cDNA of YB-1 and thus would contain SEQ ID NO: 20, which is targeted to the coding region of YB-1. Ohga et al. do not teach the use of multiple oligonucleotides targeted to YB-1.

Branch teaches on page 48 that a strategy to increase specificity of antisense therapy involves directing multiple antisense compounds to different sites within a particular target RNA.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Ohga et al. of inhibition of YB-1 with an antisense oligonucleotide by using multiple oligonucleotides as taught by Branch. One would have been motivated to do so by Branch, who teaches that use of multiple oligonucleotides is one way of increasing specificity of antisense therapy. One of ordinary skill in the would have had a reasonable expectation of success in modifying the teachings of Ohga et al. to use multiple oligonucleotides because the synthesis of oligonucleotides is well known and routine in the art.

Thus, the invention of claims 6, 9, 33, 35 and 36 would have been obvious, as a whole, at the time of invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now

contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Examiner
Art Unit 1635

TV
March 3, 2006

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